J Surfact Deterg (2014) 17:1141–1149
DOI 10.1007/s11743-014-1628-8

ORIGINAL ARTICLE

Amide-Based Surfactants from Methyl Glucoside as Potential Emulsifiers

Salih Mahdi Salman · Thorsten Heidelberg · Rusnah Syahila Duali Hussen · Hairul Anuar Bin Tajuddin

Received: 20 January 2014 / Accepted: 18 July 2014 / Published online: 15 August 2014

Abstract A series of amide-linked surfactants from methyl glucoside was synthesized and investigated for their potential use as water-in-oil emulsifiers. The synthetic concept combined a nucleophilic substitution approach with a Staudinger coupling of the intermediate azide. Both straight and Guerbet-type branched fatty acids ranging from C_8 to C_{16} were applied. All surfactants exhibited very high Krafft temperatures, which were related to the amide linkage and exclusively formed the hexagonal H_1-phase. The Guerbet C_{16} surfactant enabled the formation of a stable water-in-oil gel at ambient temperature, which, however, required heating to form the corresponding fluid emulsion.

Keywords Carbohydrate surfactant · Hexagonal phase · Alkyl-branched glycolipids · Water-in-oil emulsion · Staudinger reaction · Renewable resources

Introduction

Environmental issues and limitation of petrochemical resources are continuously shifting the focus of chemical product development towards the utilization of biological resources. Although most surfactants [1] are already based on natural lipids, the biomaterial only accounts for the hydrophobic domain. Improved skin compatibility and superior emulsion stability towards pH and ionic strength, has created considerable interest in non-ionic surfactants [2]. Most commonly used are polyethylene glycol ethers, whose hydrophilic domain derives from ethylene oxide, a petrochemical resource. Biological derived alternatives cover various glycolipids, in which the hydrophilic domain originates from carbohydrates.

Glycolipids can be classified into three major classes based on the linkage between the sugar and the hydrocarbon domain. Most chemical resistant are glycosides. Common examples are APG, or alkyl poly-glucosides [3, 4]. However, the reduction of natural fatty acids into the corresponding alcohols and their subsequent glycosylation render these surfactants comparably expensive. More economic are sugar esters [5, 6], which can be accessed easily by an enzymatic process [7, 8]. The cost advantage of these carbohydrate-based surfactants comes at a price of low chemical stability, due to easy hydrolysis of the ester bond in both acidic and basic media. Considerably more stable, yet still economic, are sugar-based amides. Extensive experience in peptide synthesis has led to well-established processes for the formation of amides [9, 10]. However, amino-sugars, like glucosamine, are comparably expensive starting materials.

In view of preparing a new surfactant for water-in-oil emulsions based on renewable resources, we searched for a suitable carbohydrate precursor. The main target was an emulsifier for hydro-fuel [11], in which water enhances the efficiency of fuel by creating additional pressure upon combustion while cooling the engine at the same time. Besides this, cosmetic oil based formulations are

Electronic supplementary material The online version of this article (doi:10.1007/s11743-014-1628-8) contains supplementary material, which is available to authorized users.

S. M. Salman · T. Heidelberg (✉) · R. S. D. Hussen · H. A. B. Tajuddin
Faculty of Science, Chemistry Department, University of Malaya, Lembah Pantai, 50603 Kuala Lumpur, Malaysia
e-mail: heidelberg@um.edu.my

S. M. Salman
Faculty of Medicine, Chemistry Department, University of Diyala, Diyala Governorate, Republic of Iraq

interesting applications as well. Economy aspects combined with a request for a limited number of hydroxyl groups suggested methyl glucoside. The glycoside can easily be obtained from glucose and is among the least expensive carbohydrate building blocks that are commercially available [12]. The glycosylation blocks the anomeric hydroxyl group, thus improving oxidation resistance, while reducing the surfactant's polarity at the same time. The latter enhances the solubility in non-polar environment, which is favorable if oil based media are targeted. An alternative usage of a pentose, e.g., xylose, more than doubles material costs and, therefore, is uneconomic.

Amide-based surfactants from methyl glucoside can utilize the sugar either as uronic acid [13] or as amino [14] component. In view of the common source for the hydrophobic domain, i.e., fatty acids, the latter approach was chosen.

Materials and Methods

Starting materials and reagents of synthesis grade were obtained from various commercial sources and used without further purification. The same applies for solvents, which were of AR grade. Purification of glycolipids and their precursors applied column chromatography using the flash technique, while no purification was required for fatty acid derivatives.

The synthetic scheme, see Fig. 1, closely followed a previously reported sequence for lower molecular homologues [14]. The introduction of the amino-group on a glycoside is most easy applied on the primary hydroxyl group. A suitable way is a substitution with sodium azide [15]. The primary alcohol can be activated as halide by treatment of methyl glucoside, **1**, with the corresponding halogen succinimide, for economic reason preferably the chloro-compound NCS, and triphenylphosphine in DMF [16]. Alternatively, the azide can be introduced in a one-pot procedure applying sodium azide in the presence of triphenylphosphine and carbon tetrabromide [17]. Subsequent acetylation of the remaining secondary hydroxyl groups, see scheme in Fig. 1, simplifies the purification of intermediates and avoids possible side reactions during the Staudinger coupling [18–20] of the azido-glucoside **2** [15] with the fatty acid derivative. While the Staudinger reaction may be applied to couple organic azides directly with carboxylic acids [21], **3**, better conversions can be obtained by applying the corresponding acid chlorides [22], **4**, which are accessible by simple treatment with oxalyl chloride [23]. Mild hydrolysis under Zemplén conditions [24] enables the selective removal of acetate protection groups without side effects on the amide.

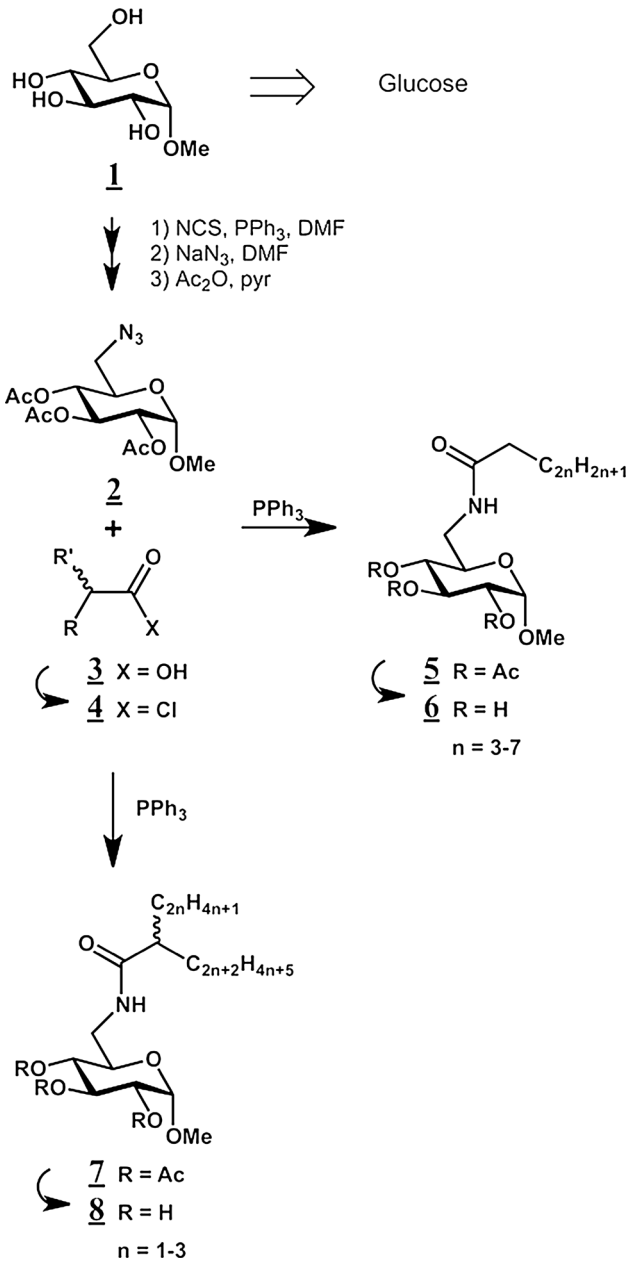

Fig. 1 Synthesis scheme for amide-based surfactants from methyl glucoside

All surfactants were spectroscopically analyzed in acetylated as well as in deprotected form. Structural identities are based on NMR spectra (^{1}H and ^{13}C, recorded on 400 MHz spectrometers) and high-resolution mass spectrometry, which were recorded on an LCMS with electrospray ionization. In order to assign ^{13}C-NMR signals, exemplary HMQC spectra were recorded for both protected and unprotected surfactants of each series. Chemical purities were confirmed by elemental combustion analysis (CHN). Due to instrumental limitations and high environmental humidity the hydrogen data were consistently to

high, whereas both carbon and nitrogen contents confirmed the purity of the material.

The thermotropic behavior of the material was studied by differential scanning calorimetry (DSC) in a replicated heating–cooling cycle at a heating/cooling rate of 10 °C min^{-1}. Phase assignments are based on the transition enthalpies, but confirmed by optical polarizing microscopy (OPM) images. The textures were obtained upon cooling from the isotropic liquid. Lyotropic phases were investigated using the contact penetration technique under OPM observation [25, 26]. Besides water, long chained surfactants were also contacted with methyl laurate to access the behavior in an oil-based environment. The determination of Krafft points applied slow heating of 4 mL samples of the surfactant in water in an oil bath under moderate stirring until the mixture cleared. Critical micelle concentrations were determined based on surface tension measurements over a wide concentration range. Calculations applied linear regressions of the surface tension as function of the logarithmic concentration for the concentration depending region as well as for the plateau at high concentration. Surface tension measurements were performed using the du Nouy ring method in five replicates with a maximum standard deviation of 0.1 mN m^{-1}.

Molecular modeling was executed on the octanoyl amide **6-8** as well as for a few reference compounds in GAUSSIAN 09™ using density function B3LYP with basis set 6-31G without consideration of a solvent and tight conversion criteria. In order to evaluate different sugar conformations, input configurations differing in intramolecular hydrogen bonding were compared. The structure of the branched chain surfactant **8-8/4** was obtained based on the DFT-based structure of **6-8** after modification and subsequent minimization of the alkyl chain region in MOPAC™ using AM-1.

Emulsion studies applied methyl laurate with 5 % water and about 0.5 % surfactant content. Homogenization was achieved by mechanical perturbation and ultrasonication at elevated temperature in 5-mL samples.

Experimental Procedures

(I) Fatty acid activation: Fatty acid **3** was dissolved in chloroform. Oxalyl chloride (1.5 equiv) was added and the reaction was warmed to 60 °C for a few hours. Evaporation of solvent and excess reagent furnishes the clean acid chloride **4**.

(II) Staudinger Coupling [14]: A solution of fatty acid chloride **4** (1.6 equiv) in dichloromethane was added drop wise to a mixture of azide **2** [15] and triphenylphosphine (1.2 equiv) in the same solvent. Stirring at room temperature was continued for about 7–15 h, by which the reaction had turned into a cloudy solution. The solid was filtered off and the solution was washed with 5 % sodium hydrogen carbonate solution, dried over magnesium sulfate and evaporated to dryness. The resulting syrup was chromatographed on silica gel with hexane/acetone 6:1 to afford the amide **5** or **7**, respectively, as white crystals.

(III) Deacetylation: Acetylated amide **5** or **7**, respectively, was dissolved in methanol and treated with a catalytic amount of sodium methoxide. After stirring for 24 h at room temperature the mixture was neutralized with Amberlite IR 120 (H^+). The resin was filtered off and the methanol was evaporated to furnish the target surfactant **6** or **8**, respectively, in almost quantitative yield.

Results and Discussion

Amide linked surfactants from methyl glucoside were obtained in overall yield of almost 50 % based on the carbohydrate starting material. This is in good agreement with the previously reported synthesis of **8-6** and lower molecular weight analogs [14]. Both straight and α-branched (Guerbet) fatty acids, ranging from 8 to 16 carbons, were applied without significant differences with respect to the process efficiency. Chromatographic purification was required, in particular to remove the phosphinoxide formed during the initial substitution of the hydroxyl group at C-6 as well as in the Staudinger-based coupling of the carbohydrate and the fatty acid. Combustion analyses of the acetylated intermediates **5** and **7** confirmed high purity of the material, as carbon and nitrogen contents matched the calculated values, whereas the NMR-spectra of the final surfactants, **6** and **8** respectively, proved the complete removal of the protection groups. The NMR data were in good agreement with previously reported values for lower homologues [14]. However, due to the application of different solvents for the unprotected surfactants, **6**, the data deviate slightly.

Table 1 shows characteristic thermodynamic data for the surfactant series **6** and **8**. A comparison of the melting point of **6-8** with previously reported data [14] indicates a minor depression, thus suggesting traces of impurities, although these could not be detected otherwise. Alternatively the presence of hydrate water in the literature reported compound might account for the higher melting point. While the current material was dried in a vacuum oven at 50 °C over phosphorous pentoxide prior to the determination of the melting point, no special precautions are reported in the literature. DSC analysis for higher

Table 1 Overview of synthesis and thermal behavior

Compound	n	Lipid domain		Overall yield (%)	Dehydration		mp	
					T (°C)	ΔH (kJ mol^{-1})	T (°C)	ΔH (kJ mol^{-1})
6-8	3	C_8	Straight	47	–[a]	–[a]	131[b]	32
6-10	4	C_{10}		48	120	12	139	27
6-12	5	C_{12}		46	125	23	144	37
6-14	6	C_{14}		45	126	28	147	42
6-16	7	C_{16}		45	129	30	147	43
8-6/2	1	C_8	Branched	45	–[a]	–[a]	185	30
8-8/4	2	C_{12}		43	–[a]	–[a]	171	31
8-10/6	3	C_{16}		44	–[a]	–[a]	154	25

[a] Vacuum dried at elevated temperature

[b] Ref. 135 °C [14]

Table 2 Overview of surfactant properties

Compound		Lipid domain		T_K (°C)	CMC			Phases in water @ 30 °C
No	n				c (mmol L^{-1})	T (°C)	γ (mN m^{-1})	
6-8 [14]	3	C_8	Straight	65	34	70	32	H_1
6-10	4	C_{10}		70				H_1
6-12	5	C_{12}		80	0.27	80	30	H_1
6-14	6	C_{14}		95				H_1
6-16	7	C_{16}		100				H_1
8-6/2	1	C_8	Branched	55				H_1
8-8/4	2	C_{12}		75	0.62	80	31	H_1
8-10/6	3	C_{16}		100				H_1

homologues 6–10 to 6–16 revealed hydrate water, which consistently evaporates at about 120 °C, while no water was found for the branched amides **8**. The reason for the different behavior is a change in the operating scheme due to lack of access to the drying equipment.

Unlike alkyl glucosides, none of the amide surfactants exhibited thermotropic liquid crystalline behavior. This corresponds with high melting temperatures of the compounds, see Table 2. The melting enthalpy probably rather reflects a transition from a gel-phase to the isotropic liquid than a transition from a crystalline solid. This in line with the OPM images in Fig. 2, which show a continuous pattern rather than sharp crystalline domains. The textures suggest a (hexagonal) columnar geometry. The behavior of the straight surfactant type **6** deviates distinctly from the Guerbet analogue **8**. While melting points for the former increase with growing chain length, apparently approaching a plateau, increasing chain length lowers the melting point for the latter. However, both series may approach the same saturation value. The high melting point indicates strong intermolecular interactions, which, according to the trend behavior, must be related to the carbohydrate domain of the surfactant. Hydrogen bonding, involving the amide as either acceptor and/or donor is a likely explanation.

In line with a previous report [14], Table 2 indicates very high Krafft temperatures for all surfactants, thus confirming a high tendency of the carbohydrate domain to 'crystallize'. The Krafft temperature increases with the chain length for both straight and branched glycolipids. The slightly lower values for the biantennary series **8** refer to better solubility due to the compactness of the hydrophobic domain. This literature known trend [27, 28] is also reflected in the increase of the CMC for the branched C_{12}-glycolipid **8-8/4** compared to its straight analogue **6-12**, see Fig. 3. The value of the latter is in good agreement with an expected increase of factor ten for two methylene groups [29] and the previously reported data for **6-8** [14]. The CMC investigation was limited to the C_{12} glycolipids, as the shorter chained surfactant are neither expected to exhibit good performance for an oil based media, nor economic due to low contents in renewable resources. Longer chained homologues, on the other hand, are extremely difficult to measure, due to the high Krafft temperature.

The surface tensions at the CMC for both C_{12}-surfactants are slightly below that preciously reported for **6-8** [14]. As the temperature for both investigations is very similar, its is assumed that the difference accounts for the increased chain length. A comparison of the surface tension at the CMC for **6-12** with a previously reported ester analog [30] indicated a significant reduction of surface activity for the amide. This corresponds with a decreasing

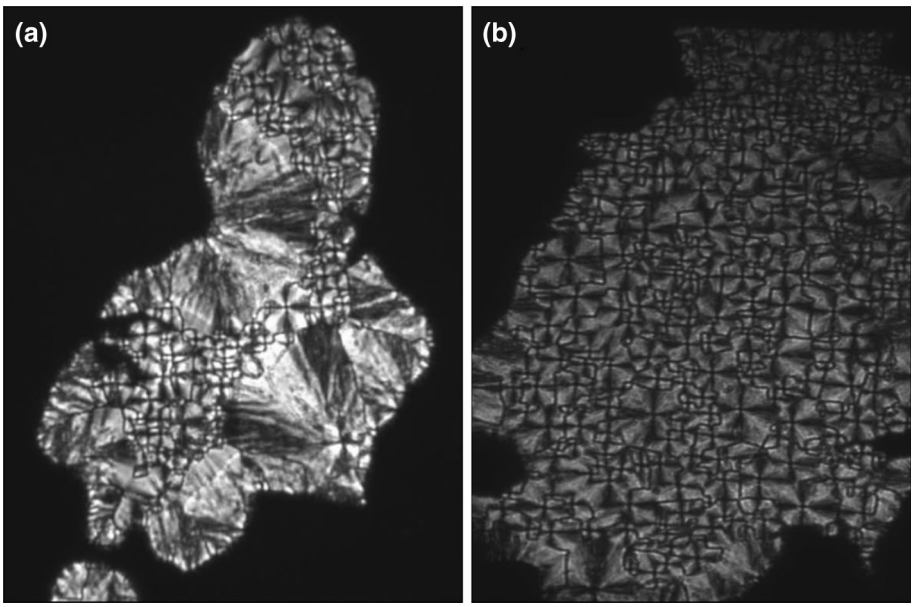

Fig. 2 OPM textures for **6-16** (**a**) and **8-10/6** (**b**) obtained upon cooling of the isotropic melt

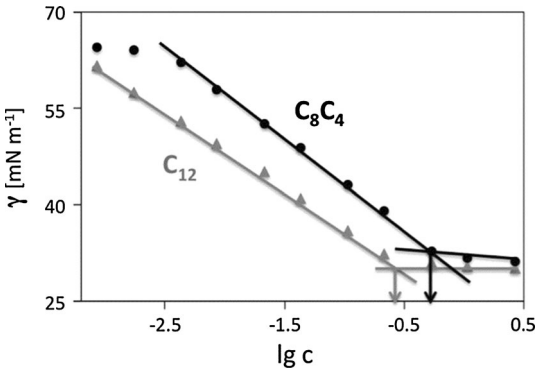

Fig. 3 CMC investigation for the C_{12}-surfactants **6-12** and **8-8/4**

CMC by factor two, thus indicating significantly stronger inter-molecular interactions for the amide than for the ester. It is assumed that these are mediated through hydrogen bonding involving the amide linkage.

The lyotropic investigation of the surfactants in water showed exclusive formation of the hexagonal phase, H_1, as shown in Fig. 4. It was difficult to obtain characteristic textures. With focus on the high Krafft temperature, samples were heated to improve the quality of the texture. No indication for lamellar phases (esp. myelin figures) have been found in any penetration scan. Overall the textures are more fitting for a hexagonal phase. This is an indication for the H_1-phase, as the inverse H_2-phase can only be formed for larger branched surfactants, like **8-10/6**. The complete absence of the lamellar phase demonstrates the dominance of the carbohydrate domain for the molecular surface area, which is in contrast to a previously found trend for Guerbet-type alkyl β-glucosides [31].

In view of the unusual phase behavior in water, a molecular modeling study was performed, aiming for a packing theory [32] based explanation. Figure 5 shows the optimized conformation for **6-8**. Instead of a previously suggested five-membered ring hydrogen bond of the amide NH with the ring oxygen of the carbohydrate [14], an eight-membered ring hydrogen bond between the hydroxyl group at C-4 and the amide carbonyl was found. This hydrogen bond leads to a tilt of the hydrocarbon chain relative to the carbohydrate ring, thus increasing the molecular surface area significantly. Due to the applied vacuum conditions for the modeling, H-bonding based structural features may differ in aqueous environment. Therefore the DFT study was extended applying three vacuum-minimized structures as summarized in Table 3, involving intra-molecular hydrogen bonds between the hydroxyl group at C-4 and the amide carbonyl, the amide NH and O-4 as well as the amide NH and the ring-oxygen O5, respectively, as input conformation and implementing the aqueous environment as continuous medium resembled by the solvents dipole moment. Unfortunately all calculation failed to converge. However, the hydrogen bonds between the 4-hydroxy group and the amide carbonyl as well as between amide NH and the O-4 remained intact during the entire calculation, while the previously proposed hydrogen bond between the amide NH and the ring oxygen broke. This is consistent with significantly lower energy for the first two conformations, as shown in Table 3, and supports the assumption of stability of these two hydrogen bonds in an aqueous environment. Based on the lower total energy for the structure involving the 8-ring H-bond under vacuum conditions, it can be assumed that the minimized structure displayed in Fig. 5 reflects the optimum conformation in an

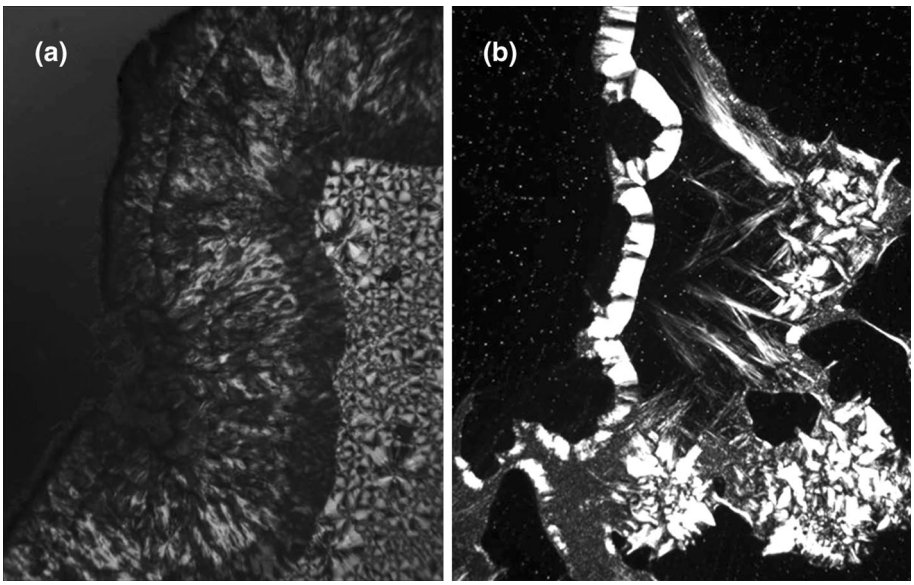

Fig. 4 Contact-penetration with water; (**a**) **6-8** @ rt, (**b**) **8-10/6** @ rt

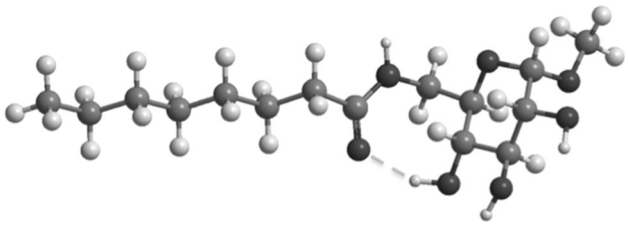

Fig. 5 Intramolecular H-bonding leads to tilting of headgroup, thus increasing the molecular surface area

Table 3 Relative stability of carbohydrate conformations for amide **6-8**

Intra-molecular H-bonding		Ring size	Total energy	
H-Donor	H-acceptor		RMS (AU)	ΔE (kJ mol^{-1})
4-OH	C=O	8	−1,094.834	ref.
NH	O-4	6	−1,094.832	3.9
NH	O-5	5	−1,094.821	33.4

aqueous environment as well. Figure 6 demonstrates the dominance of the sugar head-group on the molecular surface area based on the optimized conformation for both, the straight glycolipid type **6** as well as the branched analog **8**. The tilting effect is comparable with the increase of molecular surface area when changing an equatorial glycoside **10β** into the axial analog **10α**, see Fig. 7.

The simulation results match a trend based on literature derived, surface tension based molecular surface areas for anomeric alkyl glucosides. These indicate a significantly increased value for the α-anomer (49 Å^2 [33]) compared to β-analogues (38 Å^2 [34], 43 Å^2 [27]). The latter is in reasonable agreement with X-ray based [35] data indicating molecular surface areas of 35 Å^2 for aqueous octyl β-glucoside formulations in the lamellar phase [36]. The reported value for **6-8** (49 Å^2) [14] perfectly matches that of the α-glucoside, this way confirming the simulation based expectation of similar molecular surface areas for core structures **6** and **10α**. The exclusive formation of hexagonal phases for **6** and **8**, however, cannot solely be related to the molecular surface area of the carbohydrate head group, as α-glycosides, which resemble the molecular

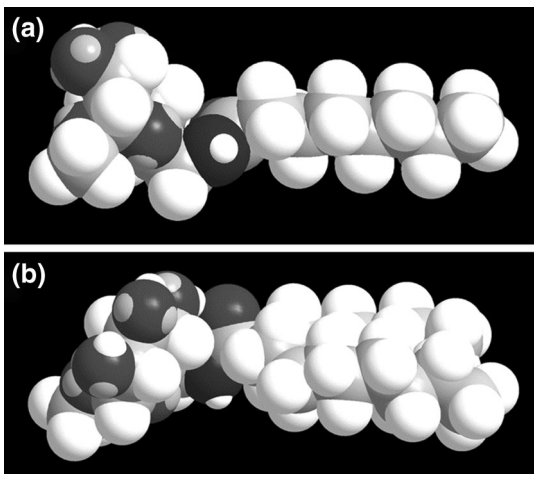

Fig. 6 Molecular models for **6-8** and **8-10/6**

shape of **6** closely, form lamellar phases in contact with water [35]. It is therefore believed that, unlike for **10α**, **6** and **8** exhibit specific, directed interactions, which account for a packing based increase of the molecular surface area.

The high Krafft temperature of the surfactants may be explained by strong intermolecular hydrogen bonding.

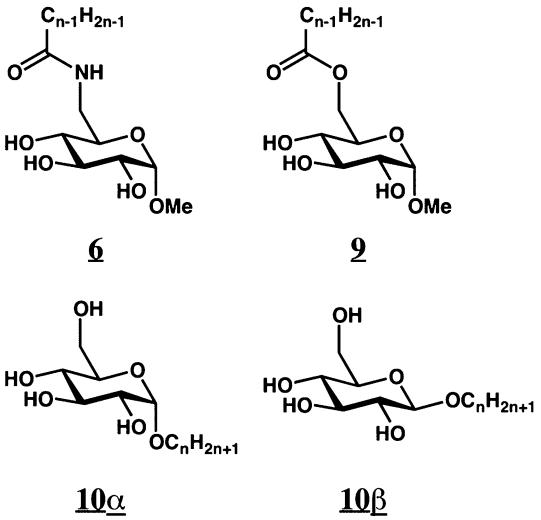

Fig. 7 Molecular structure comparison for various glucoside-based surfactants

Although the conformations for **6** and is oxygen analog **9** are almost identical, including the eight-membered ring hydrogen bond that accounts for the tilting of the head-group and the large molecular surface area, the Krafft temperature of ester **9** [30] remains significantly lower than the one of amide **6** [14]. This strongly suggests the involvement of the amide hydrogen in the hydrogen bonding. Figure 8 shows a possible interaction scheme, which is related to the intra-molecular H-bonds responsible for the secondary structure of proteins. The intra-molecular hydrogen bond involving the hydroxyl-group at C-4 increases the polarity of the NH bond, thus giving rise to strong intermolecular interactions of neighbored surfactants. Experimental indications for strong intermolecular interactions of surfactant molecules are found in the consistent patterns of mass spectra for **6** and **8**. Besides the expected signals for [M+H] and [M+Na], Fig. 9 shows an intense peak at [2M+Na], which reflects the intermolecular interactions. While the [M+H] signal is significantly larger than the corresponding [2M+H] peak, the opposite behavior applies for the sodium adducts. An explanation of this behavior is a destabilization of the intermolecular H-bonding upon protonation, which is expected to happen on the amide.

In order to evaluate the potential of the surfactants as stabilizer for water-in-oil emulsions, a contact penetration scan with methyl laurate was performed. The hydrophobic solvent was selected based on potential application for hydro-fuel from renewable sources, i.e. biodiesel. Figure 10 shows that the surfactant in growing into the oil phase, thus suggesting a good interaction of the surfactant with the oil and a potential for the intended application. With respect to highest expected solubility of the surfactant in the oil, only compounds with hydrocarbon domains

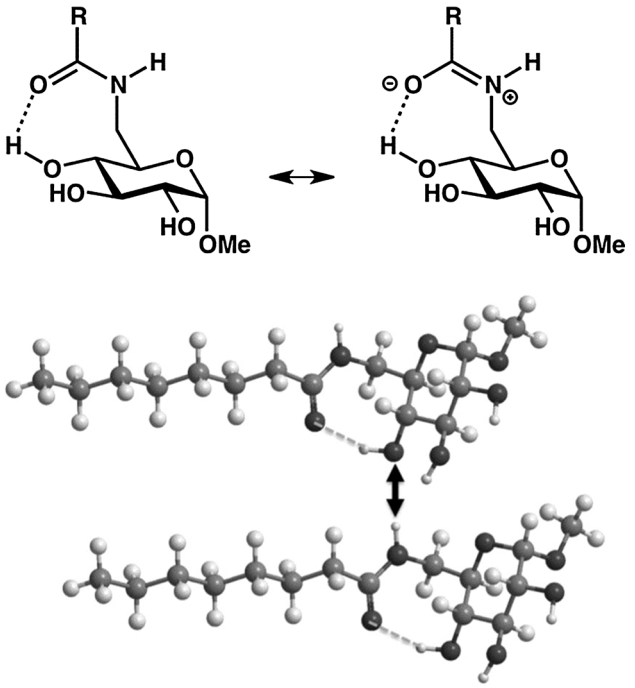

Fig. 8 Amide-based H-bonding due to intramolecular H-bonding increasing intermolecular cohesion

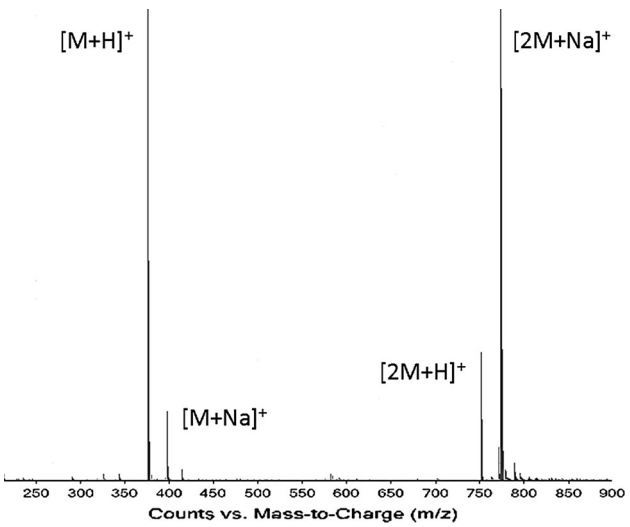

Fig. 9 Typical pattern for mass-spectra of 6-acylamino glucoside surfactants

involving 14 and 16 carbons, i.e., **6-14**, **6-16** and **8-10/6**, were selected for a preliminary formulation study. The straight hydrocarbon surfactants led to phase separation within a week (3 days for the C_{14} compound, while the C_{16} analog required about 7 days). No separation was observed for the branched C_{16} surfactant **8-10/6** within an observation period of several weeks. However, the initially fluid emulsion forms a gel after about three weeks, which requires heating above 40 °C to liquefy again.

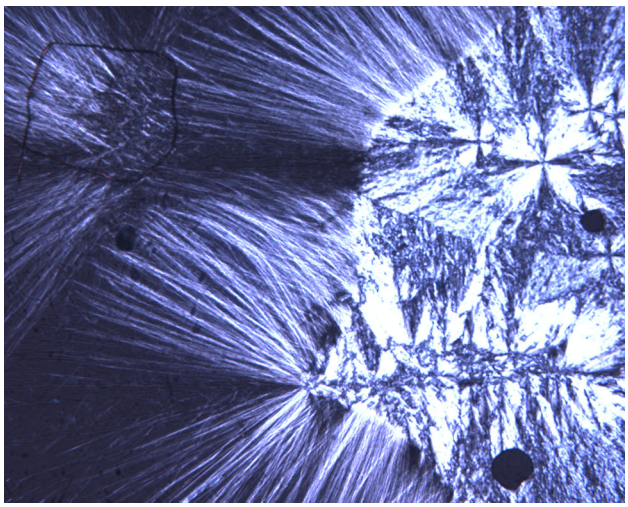

Fig. 10 Contact penetration of **6-16** with methyl laurate @ 50 °C

Conclusion

Amide-based glycolipids from methyl glucoside are easily accessible surfactants from renewable resources. The synthesis, however, requires several steps, thus rendering the surfactants rather expensive. Although the material exhibits good interaction with lipid-based oil, like methyl laurate, only the alkyl-branched type **8** enables the formation of a stable water-in-oil emulsion. The reason lies in the large, carbohydrate-dominated surface area of the surfactant, which originates from a tilting of the hydrocarbon chain towards the cyclic carbohydrate due to the intramolecular H-bonding of the 4-hydroxy-hydrogen to the amide carbonyl. Packing theory [32] considerations predict a hexagonal phase H_1 as favorable assembly geometry for the single chained surfactant type **6**. This curvature, however, does not match the requirements of a reverse phase, which forms the basis for oil-based emulsions, thus formulated emulsions separate. Only chain branching combined with longer chain lengths enables a balance of the surface areas of the surfactant antipodes, leading to stable water-in-oil emulsions. Strong intermolecular interactions of the head group, which are related to the primary amide structure, lead to high Krafft temperatures, causing emulsions to solidify in a gel. Therefore, the surfactant applications as emulsifier for bio-diesel based hydro-fuel would require preheating of the fuel.

The dominating amide interaction suggests possible improvements on the Krafft temperature, if the 6-amino-glucoside precursor is N-alkylated prior to the introduction of the fatty acid, thus leading to an *N*-branched glycolipid, rather than the current *C*-branched surfactant **8**. This structure type has been reported in life-science-related patents [37], whereas its application potential for hydro-fuel application has not been investigated. Of course, this requires a change in the synthesis scheme, as the Staudinger reaction is not suitable any more. However, such an approach would be in line with improved resource accessibility, as an economic access to the C_{16}-Guerbet fatty acid from biomaterial is currently not available.

Acknowledgments This work was supported by the University of Malaya under research grants PS382-2010B, RP024-2012B and RG264-13AFR.

References

1. Knepper TP, Berna JL (2003) Chapter 1 surfactants: properties, production and environmental aspects. Compr Anal Chem 40:1–49
2. Hepworth P (2006) Non-ionic surfactants. Chem Tech Surfactants 133–152
3. von Rybinski W (1996) Alkyl glycosides and polyglycosides. Curr Opin Colloid Interface Sci 1:587–597
4. Luders H (2000) Synthesis of alkyl glucosides and alkyl polyglucosides. Surfactant Sci Ser 91:19–75
5. Allen DK, Tao BY (1999) Carbohydrate-alkyl ester derivatives as biosurfactants. J Surf Det 2:383–390
6. Hill K, Rhode O (1999) Sugar-based surfactants for consumer products and technical applications. Lipid 101:25–33
7. Chang SW, Shaw JF (2009) Biocatalysis for the production of carbohydrate esters. New Biotech 26:109–116
8. Gumel AM, Annuar MSM, Heidelberg T, Christi Y (2011) Lipase mediated synthesis of sugar fatty acid esters. Proc Biochem 46:2079–2090
9. Albericio F, Chinchilla R, Dodsworth DJ, Najera C (2001) New trends in peptide coupling reagents. Org Prep Proced Int 33:203–263
10. Lloyd-Williams P, Albericio F, Giralt E (1993) Convergent solid-phase peptide synthesis. Tetrahedron 49:11065–11133
11. Salatov VG (2011) Method for preparing an emulsion, system and apparatus for carrying out said method. PCT Int. Appl. WO 2011016742A2
12. Bols M (1996) Carbohydrate Building Blocks. Wiley, New York
13. Fieser M, Fieser LF, Toromanoff E, Hirata Y, Heymann H, Tefft M, Bhattacharya S (1956) Synthetic emulsifying agents. J Am Chem Soc 78:2825–2832
14. Maunier V, Boullanger P, Lafont D, Chevalier Y (1997) Synthesis and surface-active properties of amphiphilic 6-aminocarbonyl derivatives of D-glucose. Carbohydr Res 299:49–57
15. Hanessian S, Ducharme D, Capmau ML (1978) A one-flask preparation of methyl 6-azido-6-deoxy-α-D-hexopyranosides. Carbohydr Res 63:265–269
16. Hanessian S, Ponpipom MM, Lavellee L (1972) Procedures for the direct replacement of primary hydroxyl groups in carbohydrates by halogen. Carbohydr Res 24:45–56
17. Blanco JLJ, Fernandez JMG, Gadelle A, Defaya J (1997) A mild one-step selective conversion of primary hydroxyl groups into azides in mono- and oligo-saccharides. Carbohydr Res 303:367–372
18. Staudinger H, Hauser E (1921) Über neue organische Phosphorverbindungen IV: phosphinimine. Helv Chim Acta 4:861–886
19. Gololobov YG, Zhmurova IN, Kasukhin LF (1981) Sixty years of Staudinger reaction. Tetrahedron 37:437–472
20. Gololobov YG, Kasukhin LF (1992) Recent advances in the Staudinger reaction. Tetrahedron 48:1353–1406

21. Czifrák K, Hadady Z, Docsa T, Gergely P, Schmidt J, Wessjohann L, Somsák L (2006) Synthesis of *N*-(β-D-glucopyranosyl) monoamides of dicarboxylic acids as potential inhibitors of glycogen phosphorylase. Carbohydr Res 341:947–956
22. Boullanger P, Maunier V, Lafont D (2000) Synthesis pf amphiphilic glycosyl amides from glycosyl azides without reduction to glycosyl amines. Carbohydr Res 324:97–106
23. Daubert BF, Fricke HH, Longenecker HE (1943) Unsaturated synthetic glycerides I: unsymmetrical monooleo-disaturated triglycerides. J Am Chem Soc 65:2142–2144
24. Zemplen G, Gerecs A, Hadacsy I (1936) Über die Verseifung acetylierter Kohlenhydrate. Ber Dt Chem Ges 69B:1827–1829
25. Rendall K, Tiddy GJT, Trevathan MA (1983) Optical microscopy and nuclear magnetic resonance studies of mesophases formed at compositions between hexagonal and lamellar phases in sodium n-alkanoate + water mixtures and related surfactant systems. J Chem Soc Faraday Trans 1(79):637–649
26. Laughlin RG (1992) The role of swelling methods in surfactant phase science: past, present and future. Adv Colloid Interface Sci 41:57–79
27. Nielson F, Södermann O, Johanson I (1998) Four different C8 alkylglucosides. Anomeric effects and the influence of straight vs. branched hydrocarbon chains. Colloid Interface Sci 203:131–139
28. Heidelberg T, Chuan R, Chie NC, Anwar SA, Hashim R (eds) (2009) Synthesis and surfactant study on isomeric octyl glucosides. Mal J Sci 28:105–113.
29. López O, Cócera M, Parra JL, de la Maza A (2001) Influence of the alkyl chain length of alkyl glucosides on their ability to solubilize phosphatidylcholine liposomes. Colloids Surf A 193:221–229
30. Ariffin MFK, Annuar MSM, Heidelberg T (2013) Surfactant synthesis via lipase esterification of methyl a-D-glucopyranoside with selected aliphatic carboxylic acids. J Surfact Deterg. doi:10.1007/s11743-013-1529-2 (in print)
31. Brooks NJ, Hamid HAA, Hashim R, Heidelberg T, Seddon JM, Conn CE, Husseini SMM, Zahid NIM, Hussen RSD (2011) Thermotropic and lyotropic liquid crystalline phases of Guerbet branched-chain D-glucosides. Liq Cryst 38:1725–1734
32. Israelachvili JN, Mitchel DJ, Ninham BW (1976) Theory of self-assembly of hydrocarbon amphiphiles into micelles and bilayers. J Chem Soc Faraday Trans II 72:1525–1568
33. Matsumara S, Imai K, Yoshokawa S, Kawada K, Uchibori T (1990) Surface activities, biodegradability and antimicrobial properties of n-alkyl glucosides, mannosides and galactosides. J Am Oil Chem Soc 67:996–1001
34. Kjellin URM, Claesson PM, Vulfson EN (2001) Studies of *N*-dodecyllactobionamide, maltose 6′-*O*-dodecanoate and octyl β-glucoside with surface tension, surface force and wetting techniques. Langmuir 17:1941–1949
35. Sakya P, Seddon JM, Vill V (1997) Thermotropic and lyotropic phase behavior of monoalkyl glycosides. Liq Cryst 23:409–424
36. Nguan HS, Heidelberg T, Hashim R, Tiddy GJT (2010) Quantitative analysis of the packing of alkyl glycosides: a comparison of linear and branched alkyl chains. Liq Cryst 37:1205–1213
37. Kurita H, Yamagushi T, Onta T (1995) Acylaminosaccharide derivative and process for preparing the same, European patent EP 650974A1

Salih Mahdi Salman obtained both bachelor's and master's degree of science in organic chemistry from the University of Baghdad and completed his Ph.D. at the University of Malaya under supervision of Associate Professor Thorsten Heidelberg and Hariul Anuar Tajuddin in 2013. Currently he is a lecturer at the Faculty of Medicine, University of Diyala in Iraq. His interest area is organic synthesis.

Thorsten Heidelberg is an associate professor affiliated to the Department of Chemistry at the University of Malaya, Kuala Lumpur, Malaysia. He obtained his Ph.D. at the University of Hamburg, Germany. His area of expertise includes organic synthesis, molecular assembly behavior and nano-materials. His research emphasizes on carbohydrate chemistry with focus on the assembly of glycolipids, and surface functionalization of nanoparticles for potential life science applications.

Rusnah Syahila Duali Hussen is a senior lecturer at the University of Malaya and affiliated to the Department of Chemistry, where she also obtained her Ph.D. Her area of expertise covers molecular assembly and liquid crystalline behavior. A particular interest focuses on surfactant systems for emulsion-related applications and the formulation of vesicles.

Hairul Anuar Bin Tajuddin is a senior lecturer at the University of Malaya and is affiliated to the Department of Chemistry. He obtained his Ph.D. at the University of Sheffield, UK. His field of expertise is physical organic chemistry, where he studies organic reactions and investigates self- assembled monolayers.